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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/614,003	07/11/2000	Walter Gehring	7326-092	1043

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EXAMINER

KATCHEVES, KONSTANTINA T

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 12/03/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/614,003

Applicant(s)

GEHRING ET AL.

Examiner

Konstantina Katcheves

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,7-10,18,24-34,50-52,63-66 and 69-83 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-5,7-10,18,24-34,50-52,63-66 and 69-83 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5, 7-10, 18, 24-34, 50-52, 63-66 and 69-83 are pending in the present application.

Response to Amendment

Claims 1-5, 7-10, 13-15, 18-21, 24-34, 50-52, 63-66 and 69-83 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-102 of copending Application Serial No. 09/113399 for the reasons set forth in the Office Action mailed 03 April 2002.

Claims 1-5, 7-10, 13-15, 18-21, 24-34, 50-52, 63-66, 69-83 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons of record set forth in the Office Action mailed 3 April 2002.

Claims 1-5, 7-10, 13-15, 18-21, 24-34, 50-52, 63-66, 69-83 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *in vitro* methods, does not reasonably provide enablement for *in vivo* methods for the reasons of record set forth in the Office Action mailed 3 April 2002.

Claims 1-5, 7-10, 13-15, 18-21, 24-34, 50-52, 63-66, 69-83 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons of record set forth in the Office Action mailed 3 April 2002.

Response to Arguments

Claims 1-5, 7-10, 13-15, 18-21, 24-34, 50-52, 63-66, 69-83 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over copending Application Serial No. 09/113399 for the reasons of record set forth in the Office Action mailed 3 April 2002.

Applicant's arguments in traverse of the instant rejection have been considered but are not found persuasive. Applicant argues that the present claims are drawn to a method wherein a Notch pathway and a cell fate control pathway are concurrently and independently modulated. The claims of the '399 application are drawn to a method of modulating the function of a signal transduction pathway wherein that function is involved in cell differentiation (*i.e.* cell fate) by administering an agonist of Notch function. Given the broadest reasonable interpretation, the claims of the '399 application anticipate the concurrent administration of a modulator of Notch function and a modulator of cell fate. Applicant's assertion that the present claims are concurrently and independently modulated is noted. The claims, however, recite that they are concurrently modulated and does not even imply that they are independent. Therefore, given the broadest reasonable interpretation of the instant claims and the claims of the copending application, the present claims are anticipated by the '399 application such that the claimed subject matter is not patentably distinct and that issuance of a patent on both these applications would provide unjustified extension of the right to exclude granted by a patent.

The rejections of claim 1-5, 7-10, 13-15, 18-21, 24-34, 50-52, 63-66, 69-83 under 35 U.S.C. 112, first paragraph are maintained for reasons already of record. Applicant responded to

both rejections under the enablement requirement of 35 U.S.C. 112, first paragraph in combination in Paper No. 11 file 11 September 2002. For the purposes of consistency, clarity and efficiency, Examiner rebuts Applicant's remarks in the same format.

The present claims relate broadly to a method of altering cell fate by manipulating Notch pathway function and the function of a cell fate control gene pathway. Applicant characterizes the invention of the instant claims as requiring a modulator of cell fate that is not an agonist or antagonist of Notch, but is one used in conjunction with an agonist or antagonist of Notch. As discussed above in reply to Applicants arguments rebutting the pending double patenting rejection, there is not recitation of a limitation requiring both a modulator of Notch and a modulator of a cell fate pathway that is not the Notch pathway. Therefore, Applicant's characterization of the claims is not necessarily reflected in the claim limitations.

Examiner appreciates the legal standard for enablement under the 35 U.S.C. 112, first paragraph and under *In re Wands*, 8 USPQ2d 1400, 1404 (CAFC 1988). Eight factors are considered when assessing whether the disclosure would have required the skilled artisan would be required to engage in undue experimentation. These factors include: 1) the quantity of experimentation necessary, 2) the amount of direction or guidance provided, 3) the presence of absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability of the art, and 8) the breadth of the claims.

Applicant cites *In re Angstadt*, 190 USPQ 214 (CCPA 1976) for the proposition that one need not provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing a reaction whether a product will result. According to the court if this were the case then all "experimentation" would be "undue." The holding in *In re Angstadt* is

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noted, however, is not dispositive to the present rejections under 35 U.S.C. 112, first paragraph. Applicant should note the holding of *Enzo Biochem, Inc. v. Calgene, Inc.*, 118 F.3d 1362, 52 USPQ2d 1129 (Fed. Cir. 1999) ("*Enzo*"), where claims which broadly encompass the application of a technique to all types of living organisms, including both prokaryotes and eukaryotes, were invalid for insufficient enablement because the specification set forth only three examples involving only *E. coli*. Applicant's claims and specification present a situation analogous to that posed in *Enzo*. The present claims are drawn to a method that embraces applications in all cell types and *in vitro* or *in vivo*. Applicant's disclosure, however, is limited to *Drosophila* only. Therefore, the present rejection is consistent with the holding under *Enzo*. At best, Applicant has provided an invitation to experiment in order to determine how to make use of Applicant's discovery, but guidance is not provided teaching how to use this method in any cell types or any organism. The already complex invention of altering cell fate is compounded by the extreme breadth of the claims which encompass a large number of different cell types having different developmental fates and a large number of different potential Notch antagonists which are chemically, structurally, biologically and functionally different from one another. These factors, without specific guidance from the specification as to how to use the invention, would require one of skill in the art to engage in undue experimentation. See *In re Gardner*, 427 F.2d 786, 166 USPQ 138 (CCPA 1970) (stating that the law requires that the disclosure in the application shall inform of how to use, not how to find out how to use).

Applicant argues that conservation of the Notch pathway among *Drosophila* and non-*Drosophila* cell types teaches one of skill in the art how to practice the claimed invention. Taken to its logical conclusion, Applicant asserts that its method can be practiced in any and all cell

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types and in any and all organisms. In support of this position, Applicant provides references teaching conservation of the Notch pathway between *Drosophila* and mammalian systems. Even given conservation of Notch pathway among *Drosophila* and mammalian systems, the references fail to teach which pathways will be affected. In other words, it remains unpredictable which cell fate pathways will be affected and how such that one of skill in the art could practice the claimed method in any and all cell types and any and all organisms as asserted by Applicant. Moreover, Rincon-Limas *et al.*, cited by Applicant, states that conservation does not necessarily imply conservation of function *in vivo*. See page 2169.

Applicant further argues that a “100% success rate” in gene delivery and expression of the Notch and cell fate control gene modulator is not required for practicing the claimed invention *in vivo*. Although an absolute success rate is not required, some level of predictability when considering questions of enablement is required. Applicant has failed to teach this in the specification or the art. Applicant asserts that all that is shown is a rate of delivery sufficient to achieve expression of the Notch and cell fate control gene modulators at a sufficient time and rate to result in cell fate change. Applicant has done no more than assert that the target gene can be expressed and has not provided any supporting evidence. The main obstacle to the development of gene therapy remains the targeted long-term expression of the transgene. Given the unpredictability in the art of gene therapy, as discussed in the previous office action, and no hint as to how to achieve a “sufficient” rate of delivery nor what that “sufficient” rate is, Applicant has failed to overcome the unpredictability in the art.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Konstantina Katcheves whose telephone number is (703) 305-1999. The examiner can normally be reached on Monday through Friday 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-7939 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3388.

Konstantina Katcheves

November 21, 2002


REMY YUCEL, PH.D
SUPERVISORY PATENT EXAMINER
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